Wyeth Research

Wyeth

December 9, 2002

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1060
Rockville, MD 20852

Re: Docket No. 00D-1539 – FDA Draft Guidance for Industry, Electronic Records; Electronic Signatures, Maintenance of Electronic Records

Dear Sir/Madam:

Wyeth Research is submitting written comments on the draft guidance for industry entitled, "Electronic Records; Electronic Signatures, Maintenance of Electronic Records" (67 FR 56848; September 5, 2002).

Wyeth is one of the world's largest research-based pharmaceutical and health care companies. It is a leader in the discovery, development, manufacturing, and marketing of prescription drugs and over-the-counter medication, with leading products in women's health care, cardiovascular, central nervous system, anti-inflammatory, infectious disease, hemophilia, and oncology categories, and is also a major manufacturer of preventative vaccines.

We are submitting the enclosed comments in duplicate. Wyeth appreciates the opportunity to comment on the above-mentioned draft guidance for industry.

Sincerely,

Roy J. Baranello, Jr.
Assistant Vice President
Worldwide Regulatory Affairs

00D-1539

C 20

General Comments

The Guidance should recognize that there are no guaranteed permanent technical solutions and limited commercially available solutions to meet the long-term retention requirement. Further, the guidance should include the FDA's current thinking on ways to achieve an electronic migration without unnecessary costs to industry.

Section 2 – Scope

Reference is made to the following paragraph (see lines 101-104), "When an FDA regulation requires that a record be maintained, generally the regulation specifies the period of time the record must be kept (referred to in this draft guidance as the records retention period). We intend this draft guidance to apply to the entire required retention period regardless of how actively the records are used or accessed."

Comment: The business retention period may be considerably longer than the regulatory retention period. After expiration of the regulatory retention period, a paper option seems to be implied in the guidance, but is never explicitly stated. It would be helpful for the industry to know that this may be a viable option, once the regulatory retention period is over. It could avoid a first, second or third round of electronic migration, and could save considerable resources.

We therefore suggest the addition of the following sentence at the end of the paragraph referenced above: "After expiration of the required retention period, alternative means for long-term archiving (e.g., paper or microfilm) may be used."

Reference is made to lines 105-107, "This draft guidance presents key principles and practices and addresses some frequently asked questions, but it is not intended to cover everything about maintaining electronic records."

Comment: More clarity should be provided. We are unsure whether this phrase infers that these are the minimum requirements, or that this is but one of several acceptable approaches.

Subsection 4.1 -- What Does Part 11 Require?

Comment: It is constructive to describe what constitutes the "signature manifestation information" expected. Therefore we suggest that the FDA substitute, "Accordingly, the signature manifestation information, associated with an electronic record that is subject to this requirement, must be maintained for the duration of the record retention period." (See lines 172-174) with the following sentence.

"Accordingly, the printed name of the signer, the date and time of signing and what the signature means, associated with an electronic record that is subject to

this requirement, must be maintained for the duration of the record retention period."

Subsection 5.3 – Continued Availability and Readability of Electronic Record Information Should Be Ensured

Comment: Further clarity is needed with regards to "...you should make back up copies of your most important electronic records and store them separately from the primary electronic records." (See lines 240-243.)

- The wording in the draft guidance implies that back-up records are not required for electronic records that do not fall within the "most important" category. If this is the case, language should be addressed to make this distinction more clear.
- If back-up copies are made, and a record is changed, edited or amended, which record would be the controlling record?
- Many data acquisition applications on the shop floor and in the laboratory generate a paper record concurrently with the electronic record – examples include automated inspection machines and labeling machines in production, and HPLC in the QC lab. The paper record serves as the tool with which decisions are made, such as release. In this case would the electronic record itself be the recommended 'back-up' copy? FDA's interpretation that the electronic record (including metadata) is the original should not discount the value of the paper record, which in many cases is designed to be the principle record used in the decision-making process.

Subsection 5.5 – The Ability to Process an Electronic Record's Information Throughout its Records Retention Period Should Be Preserved.

Reference is made to the opening statement (see lines 258-259), "Throughout the records retention period, the ability to process information in an electronic record should not diminish."

Comment: The regulation relates to the requirement to 'view' a record. However, a literal interpretation of the opening statement referenced above suggests that use of pdf formats for maintaining a record securely would not meet this requirement.

The guidance should be very explicit that reprocessability is only required if it is a requirement in the predicate rule. Therefore, we suggest that the sentence referenced above be replaced with "Where specifically required by predicate rule, the ability to process information in an electronic record should be maintained."

Reference is made to the following paragraph (see lines 273-282):

"Accordingly, where you could use computer technologies to search, sort, or manipulate information in an original electronic record, you should be able to use computer technologies to perform the same kinds of processing on information in the maintained electronic record. For example, if you could automatically search for words in the text of an electronic record, sort or find values in a table, or perform calculations in a spreadsheet, you should be able to process information in a like manner for the electronic record over the entire records retention period. This ability (or functionality) derives largely from the hardware and software used to extract information from the electronic record, as well as the electronic record format itself. You should include this ability among your specifications in your procedures and controls."

Comment: We recommend that this entire paragraph be revised since reprocessability is not required for copying a record in human readable and electronic form. 21 CFR 211.180(e) requires a copy for internal review – not reprocessing for FDA ease of inspection.

Also the example provided should be changed, to emphasize the reprocessing problem. Search, sort and manipulate are relatively straightforward and common capabilities that are likely to be available in a migrated system. However, the ability to regenerate chromatograms or to manipulate medical images is a processing capability that is far more difficult to maintain and is not required by the predicate rule. We, therefore request that the guidance take into account these more difficult examples, and not just the simple ones.

Subsection 5.6 -- Copying Processes Should Produce Accurate and Complete Copies.

Comment: The following text (see lines 289-293) **italicized** below appears to be extraneous text that is somewhat confusing:

"Some systems have a built-in copy verification mechanism, such as a cyclic redundancy check, that could be used to prevent an inaccurate or incomplete copy from ***Draft Guidance For Industry – Not For Implementation 12*** being made. A copy process that does not implement such a built-in error checking mechanism to prevent making an inaccurate or incomplete copy should be validated."

Subsection 6.2.1.3 -- Electronic Record Integrity Attributes Should Be Preserved.

Comment: Typically the migration process itself is automatic (i.e., not human operator controlled). The operator will take an action to start the process, but is not involved in creation of each individual new record.

While validation of the migration process would be appropriate, an audit trail for creation of each individual record in this automated process is not required (see FDA response to preamble comment #72). Therefore, we recommend that

the agency delete the following three sentences (see lines 420-426) and provide a more suitable example:

"For example, section 11.10(e) of part 11 requires that audit trails record all operator entries and actions that create, modify or delete electronic records. Where a migration, in effect, creates a new electronic record (by transforming the old electronic record) then, per section 11.10(e), the audit trail for the migrated electronic record would have to cover this creation. By adding this new creation step to the migrated audit trail carried over from the old electronic record you will help ensure a continuity of electronic record integrity."

Subsection 6.2.1.5 -- Unavoidable Differences and Losses Should Be Accounted for and Explained in the Migrated Electronic Record or New System Documentation.

Reference is made to the following sentence (see lines 452-454), "When electronic records are migrated from one system to another, we recognize that there might be unavoidable losses or changes in certain information or record attributes that do not diminish the reliability of information that is preserved and presented.

Comment: "Since there might be unavoidable losses or changes in certain information or record attributes," it is important to recognize that the essential meaning of the migrated information should not change and that only that information relevant to the essential meaning should be migrated. We therefore suggest that the following sentence be inserted after the sentence referenced above:

"The fundamental objective of the migration is to preserve the essential meaning of the information as judged by experts in the field to be equivalent to the original in the context of its stated, actual or intended use"

Comment: It should be clear that the signature itself is not migrated; what is migrated is a representation of the fact of the signature, along with a signature of testimony by a trusted third party.

Therefore we suggest that the agency replace, "The above trusted third party then applies a new digital signature (using technologies appropriate to the new system) to the migrated electronic record, " (see lines 478-480) with: "The migrated records must maintain the integrity of the association of signators (people) and records. The above trusted third party then applies a new digital signature (their own), attesting to the continued integrity of that association."

Reference is made to lines 495-497; "An electronic record that supplements the migrated electronic record should explain the correlation between old and new color representations, so that the reader would correctly interpret the information."

Comment: Given that differences between the old and new systems are documented, this appears to be an unnecessary step and one that is not typically supported by

commercial software. Consequently, this step adds substantially to the effort and cost of migration while offering limited incremental value.

Reference is made to lines 497-499, "However, text (that referred to the colors) in the migrated electronic record should not be altered because doing so would change the record content and authenticity."

Comment: We recommend that this sentence be replaced with, "The text (that referred to the colors) may be altered to be consistent with the new colors."

Transcribing of the text to refer to the *new colors* is required to preserve the essential meaning of the record in a manner that is easily understood. Requiring literal text be preserved and to be understood by humans in a convoluted fashion, especially after multiple migrations, could lead to human error of serious consequence. Migrations of text need not be any more literal than migrations of numbers that may change in literal representation from one system to the next. The key determining factor should be whether the migrated record preserves the essential meaning of the original record, i.e. judged by experts in the field to be equivalent to the original in the context of its stated, actual or intended use. Any such transcription can be documented as part of the migration process.

Furthermore, this requirement is not typically supported by commercial software.